Microbiome and other environmental factors

DEVELOP A MULTIPLEX IMMUNOFLOUORESCENCE PANEL TO IDENTIFICATION OF DISTINCT COMPLEX IMMUNE LANDSCAPES IN PLEURAL EFFUSION LIQUIDS FROM PATIENTS WITH METASTATIC LUNG ADENOCARCINOMA

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Background Lung cancer, frequently presents with advanced stage disease with approximately 15–30% of patients first diagnosed by a malignant pleural effusion (MPE). Currently, we have limited understanding of the cellular complex immune landscape compositions of MPE and how this cellular composition impacts response to therapy. Therefore, in this pilot study, we aimed to characterize the cellular composition of MPE in patients with metastatic lung adenocarcinoma (LADC).

Methods A custom multiplex immunofluorescence (mIF) panel was designed and optimized using the Opal™7 color Kit (Akoya Biosciences) against six immune markers including cytokeratins (CK), PD-L1, PD-1, CD3 CD8, and CD68 (figure 1). We selected 4 MPE cases from LADC patients to validate this mIF panel. Regions of interest (ROI) were scanned in high magnification using the multispectral microscopy Vectra Polaris (Akoya Biosciences) to capture the multiplex immune cell phenotypes and to be analyzed by the image analysis InForm software.

Results The median number of cells observed was 4,883.5 (range 1773–8292 cells). The median cells expressing CK was 15% (including tumor and mesothelial cells), CD3+ T-cell was 38%, cytotoxic T-cells CD3+CD8+ was 3%, and macrophages CD68+ was 14% (table1). The median number of CK+ cells expression PD-L1 was 1%. Additionally, the median number of CD3 T-cells expressing PD-1 or PD-L1 was in total 1%. Interestingly, with didn’t see macrophages CD68+ expressing PD-L1 in this small cohort. Furthermore, an exploratory observation showed that patients with high percentage of cytotoxic T-cells CD3+CD8+ and high percentage of macrophages CD68+ had better overall survival (table 2).

Conclusions In our cohort of MPE, we were able to assess, with extraordinary fidelity according to the antibodies included in the panel, several cell phenotypes, showing that we successfully multiplexed these biomarkers using mIF. These results demonstrate the practical scalability of this method for studying different aspects of cytological material and the data generated with the image analysis can be used to explore prognosis and potential therapeutic response in the future.

REFERENCES

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cancers, but with variable efficacy. Prior research has also suggested that systemic antibiotic (ABX) exposure may impact the intestinal microbiota and result in suboptimal ICI treatment outcomes. Our team published a systematic review and meta-analysis showing that ABX use could indeed decrease the survival of patients diagnosed with non-small-cell lung cancer (NSCLC) and treated with ICIs. The present abstract aims at updating this meta-analysis by incorporating new studies that have been published in the period ranging from September 2019 to August 2020.

Methods Medline (through PubMed), the Cochrane Library and major oncology conferences proceedings were systematically searched to identify studies assessing the impact of ABX use on the clinical outcomes of NSCLC patients treated with ICIs. Studies were found eligible for inclusion when they mentioned a hazard ratio (HR) or Kaplan–Meier curves for overall survival (OS) or progression-free survival (PFS) based on antibiotic exposure. Pooled HRs for OS and PFS and HRs for each time window of exposure were calculated.

Results 6 eligible new studies were identified between September 2019 and August 2020 while 3 other studies were updated with new information. Altogether, 27 studies reported data for OS (6,436 patients, 826 of whom coming from new studies) and 24 for PFS (3,751 patients, 786 of whom coming from new studies). The pooled HR was 1.75 (95% confidence interval [CI]: 1.38–2.23) for OS and 1.57 (95% CI: 1.28–1.92) for PFS, confirming a significantly reduced survival in patients with NSCLC exposed to ABX. The detailed analysis in subgroups based on the time window of exposure (figure 1, figure 2) suggests that the deleterious effect of ABX is stronger when the exposition happens shortly before and after the initiation of the ICI treatment.

Conclusions The update of the meta-analysis confirms the previously reported deleterious effect of ABX on ICI treatment outcomes, taking into account the latest publications in the field. The topic deserves further research to uncover if the effect will stand with 1st line use of ICI together with chemotherapy and/or other approved combinations, elucidate the mechanisms at stake and improve care of patients.

REFERENCE

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Abstract 671 Figure 1 Forest plot of hazard ratios for overall survival of patients diagnosed with NSCLC and exposed to antibiotics versus not exposed to antibiotics, according to the time window of antibiotic exposure.

Abstract 671 Figure 2 Forest plot of hazard ratios for progression-free survival of patients diagnosed with NSCLC and exposed to antibiotics versus not exposed to antibiotics, according to the time window of antibiotic exposure.